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**REMARKS****Restriction Issues**

Applicants acknowledge the current restriction requirement, and election in response thereto, including the finality thereof. Nevertheless, Applicants reiterate their request for consideration of the circumstances of the instant application, in particular the fact that it has now been in prosecution for over 9 years, in requesting that, upon indication of allowability of the nucleotide claims currently under examination, the Examiner extend examination to the corresponding protein and antibody claims, as well as method claims dependent thereon. Applicants respectfully submit that requiring Applicants to file divisional applications to pursue these claims at this time will cause Applicants to lose a minimum of 9 years of the 20 year from filing patent term for those claims, which is an undue burden compared to the burden on the Examiner to continue examination to claims which are of essentially the same scope as the nucleotide claims under examination.

**Title**

Applicants respectfully submit that they will amend the Title upon indication of allowance of the final set of claims that will be considered. It is hoped that no amendment will be needed if the Examiner will extend examination to the protein and antibody claims as well, as requested above.

**New Matter Objections**

Applicants wish to thank the Examiner for the very detailed examination of this complex application and of Applicants ongoing attempts to craft claims having a reasonable and patentable scope in view of the instant specification.

**A. Definitions of a range of substitutions**

Although Applicants have now altered the scope of the claims to focus on sequences having more particular substitutions compared to the claims submitted in the previous amendment, it is expressly asserted that this amendment should not be taken to limit the equivalents thereof to the literal scope of the claims in a claim construction analysis.

Applicants submit that the literal absence in the specification of a range of amino acid substitutions which would be acceptable in an allelic or recombinant variant, while defining the acceptable additional or substitutions to 1-5 amino acids, should not be interpreted to limit the acceptable substitutions to a single amino acid out of 93. In fact, Applicants submit that one of ordinary skill in the art, reading the specification and in view of the state of the art, would have

understood the range of acceptable substitutions to similarly have been at least 1-5, consonant with the additions and deletions permitted. Nevertheless, due to the lack of *ipsis verbis* written description of an acceptable range for number of substitutions, Applicants have alternatively used the language “one” or “at least one” in these claims. However, Applicants maintain that the reason for this amendment should not limit the scope of equivalents of the sequence in a claim construction analysis. For example, it is clear that a few or even several amino acid substitutions were contemplated by Applicants, in view of the teachings of the specification taken as a whole, so long as the resulting polypeptide retains chemokine (or, more particularly, chemotactic – see below) activity, which activity can be routinely determined by reference to assays taught in, *inter alia*, Example XII.

B. Addition, deletion and substitution variants must have chemokine/chemotactic activity

Applicants have amended the claims to more clearly define that nucleotides encoding addition, deletion and substitution variants of the polypeptide of SEQ ID NO:2 having chemotactic activity are intended, by placing that requirement in a clause separate from the definitions of the types of variants themselves. If the Examiner still believes this language is not clear, he is courteously invited to call counsel for Applicants to discuss what would be acceptable language.

C. New matter in claims 105 and 106

These claims have been amended to remove reference to the multiple specific amino acid substitutions in a PANEC-1 variant which would be permitted by comparison to the three MCP sequences, and now specifically reference sequences having a single substitution, without specifying where in the molecule it is. Nevertheless, this variant must still retain chemotactic activity. The amendments are submitted to obviate this ground of objection.

D. Objections to “non-genomic” in claim 107

Applicants have amended claim 107 to use the term “consisting of” rather than comprising to emphasize the lack of additional intervening sequences permitted in these sequences, as well as to conform other parts of the claim to the amendments made in response to the previously mentioned objections.

It is also noted that there does not appear to be any objection to the language of claim 108 relating to “encoding, without introns,” and it is assumed that this alternative to “non-genomic” was found to be acceptable, not new matter, and fully supported in the specification.

**E. New matter in the Sequence Listing/Sequence Rule Non-Compliance**

Applicants appreciate the Examiner's attention to detail, but note that the corrected Sequence Listing and CRF submitted with the response filed July 25, 2001, already corrected the Sequence Listing and CRF in accordance with the sequence in Figure 1, which supports the full length 291 nucleotide sequence encoding the full length PANEC-1 protein. Figure 1 has been amended to correct the sequence numbering as discussed with the Examiner. The Description of the Drawings in the specification has been amended to reference the SEQ ID numbers.

**Written Description Rejections under 35 U.S.C. § 112, First Paragraph**

Applicants understand the Examiner's indication that the rejection as set forth and explained in the instant Office Action "as being relaxed" refers to the concerns raised in the previous Office Action that the claims encompassed genomic sequences, including introns, and that the remainder of the comments reiterating the rejection are concerned with possible overbreadth of the claims as presented in the previous response. Withdrawal of the rejection is therefore respectfully requested.

Applicants respectfully submit that the amendments to the claims submitted herewith and discussed previously in connection with objections to alleged new matter similarly obviate the rejection for lack of written description as set forth in the Office Action. Applicants similarly submit that although Applicants have now altered the scope of the claims to focus on sequences having more particular substitutions compared to the claims submitted in the previous amendment, it is expressly asserted that this amendment should not be taken to limit the equivalents thereof to the literal scope of the claims in a claim construction analysis.

**Rejections under 35 U.S.C. § 112, Second Paragraph**

These rejections are based on the alleged vagueness and indefiniteness of the term "specifically" with respect to both the property of "specifically binds" of claimed antibodies and "specifically hybridizes" with respect to polynucleotides.

Applicants respectfully submit that these are terms of art which are well understood by one of ordinary skill in the art in the context in which these inventions are employed. For example, the term "specifically binds" with respect to an antibody would be understood to mean that the antibody would be able to bind substantially exclusively to a particular antigen (in this case, PANEC-1) in an environment in which it might be found, to the exclusion of binding to

anything else in that environment. For example, for detection of PANEC-1 in a human tissue sample, an antibody within the metes and bounds of this description would bind only to PANEC-1, and not any other chemokine, or any other protein or peptide, in that sample. It is not necessary that such an antibody would not also bind to a chimpanzee ortholog of PANEC-1, because that level of specificity would not be required to make the claimed antibody useful, as it is unlikely that a human tissue sample would be contaminated with chimpanzee tissue. Similarly, "specifically hybridizes" means that a probe sequence will hybridize specifically with its complement under sufficiently stringent hybridization conditions for a particular use; thus, in a gene expression experiment, a probe sequence should be able to distinguish between panec-1 and other chemokine polynucleotides so as to not cross-hybridize and give incorrect results. And again, specific hybridization so as to distinguish a homologous chimpanzee gene is unlikely to be required in a gene expression experiment.

Moreover, Applicants note that the ordinary dictionary meaning of "specific" is "pertaining to, characterizing, or distinguishing a species." (See the attached dictionary definition of specific). Thus, an antibody which specifically binds a polypeptide comprising SEQ ID NO:2 will be able to distinguish the SEQ ID NO:2 polypeptide from other polypeptides, and a nucleotide which specifically hybridizes with a polynucleotide of SEQ ID NO:1 will be able to distinguish the polynucleotide of SEQ ID NO:1 from other polynucleotides.

If the Examiner believes alternative claim language in addition to these clarifying remarks is needed, he is urged to call the undersigned to suggest such amendments. However, Applicants respectfully submit that the current claims are in condition for allowance, and that the rejection should be withdrawn.

### **Prior Art**

Applicants respectfully submit that the amendments made to clarify the scope of the claims now rejected over Yoshimura et al. also obviate this rejection. Applicants further submit that although Applicants have now altered the scope of the claims to focus on sequences having more particular substitutions compared to the claims submitted in the previous amendment, it is expressly asserted that this amendment should not be taken to limit the equivalents thereof to the literal scope of the claims in a claim construction analysis.

### **Informalities**

The above amendments to the specification are submitted to conform the disclosure regarding the figure numbering according to the formal drawings.

Regarding the capitalization of the terms “PANEC-1” vs. “panec-1” (and similarly the terms PANEC-2 and panec-2), Applicants submit that the terms are clearly defined in the specification to mean different things and are used consistently with those meanings throughout the specification. In particular, the capitalized version of the term means the protein (see, e.g., page 6, line 13), and the lower case version refers to polynucleotides (see, e.g., page 11, line 23). This usage is consistent in the cited section of the specification on page 17, lines 10-17. Withdrawal of the objection is therefore respectfully requested.

**CONCLUSION**

In light of the above remarks, Applicants submit that the present application is fully in condition for allowance. Early notice to that effect is earnestly solicited.

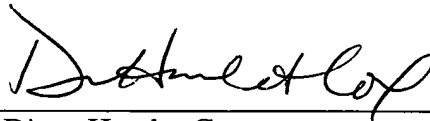
If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due or that an excess fee has been paid, the Patent Office is authorized to debit or credit (respectively) Deposit Account No. **09-0108**.

Respectfully submitted,  
INCYTE CORPORATION

Date: \_\_\_\_\_

24 Feb 2004



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